UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/387,158	08/31/99	DRYJA T	19100-021

HM12/0430

LESLIE MEYER-LEON
THE PATENT LAW GROUP
101 RIVER ROAD
SUDBURY
BOSTON MA 01776

EXAMINER	
ZEMAN, M	
ART UNIT	**PAPER NUMBER**
1631	10

DATE MAILED: 04/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/387,158	DRYJA ET AL.	
	Examiner	Art Unit	
	Mary Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-31,42 and 49-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-31,42 and 49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 1999* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)

16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .

18)☐ Interview Summary (PTO-413) Paper No(s). _____ .

19)☐ Notice of Informal Patent Application (PTO-152)

20)☐ Other:

DETAILED ACTION

Upon review of the Application, it has been decided that the Restriction requirement, mailed 12/18/00 should be withdrawn. An action on the pending claims follows.

Applicant's remarks regarding any potential terminal disclaimers, the deposits with the ATCC, and the interference in a related application have been considered.

Claims 22-31, 42 and 49-52 are pending in this application.

Drawings

Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Applicant is reminded that changes in the drawings to address the comments made by the draftsman may require similar amendments to the descriptions of those drawings.

Information Disclosure Statement

The information disclosure statement filed 12/7/99 has been entered and considered. An initialed copy of the form PTO-1449 is included with this action.

Claim Rejections - 35 USC § 112

Claims 22, 23, 29 and claim 49 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The examiner recognizes that these claims have been copied from US Patent 5,998,134 for the purposes of provoking an interference. Before an interference can be declared, all claims pending in the application must be allowable.

The metes and bounds of claim 22 are unclear. The method steps of Claim 22 appear to be an in vitro method, but the preamble of the claim suggests the method steps take place in a mammal. It would appear from the specification that some kind (what kind?) of sample should be taken from the subject, which can then be tested in the hybridization method. In view of Applicant's comments in the preliminary amendment filed 1/12/00, about the disclosed

sequences not being the consensus or wild-type sequence, what is the wild-type sequence referred to in the claim? From where is this sequence obtained? Further, it is unclear how the binding or hybridization of the wild type gene would result in the detection of the mutated gene. It would appear several discrimination steps are missing. How does one "determine" whether the sample has mutant or wild type?

In claim 23, it is not clearly stated that the cell sample comes from the human mentioned in the preamble. As the claim reads, the cell sample could be from anywhere. The "wild-type" sequence, and "determining" step of claim 23 have similar problems as in claim 22.

Claim 29 recites "normal retinoblastoma protein." What is the sequence of this "normal" protein, if it is not the one disclosed in the specification. . In view of Applicant's comments in the preliminary amendment filed 1/12/00, about the disclosed sequences not being the consensus or wild-type sequence, this limitation renders the claim indefinite.

35 U.S.C. 112, Written Description Rejection

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claims 24, 26-31, 42, and 50-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses one particular allelic variant of the RB gene (Figure 5), and a polymorphism in a repeat unit of a mutant sequence, Figure 7 discloses four discrete polymorphisms, not all of which can be detected by RFLP analysis. In the remarks in the preliminary amendment filed 1/12/00, Applicant states that the DNA sequence of Figure 5, while including a sequence for RB, is not the consensus sequence for RB. Claims 24, 26-31, 42 and 50-53 are directed to encompass gene sequences, allelic variants, encoding sequences corresponding sequences from other species, mutated sequences, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth. None of these sequences

meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the particular sequences disclosed in the specification, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171,

> 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only the particular sequences disclosed in the specification, but not the full breadth of the claim meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24-30, 42 and 50-52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-48 of U.S. Patent No.

5,853,988. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are each drawn to isolated nucleic acids comprising retinoblastoma sequences of varying types. It is noted that the '988 patent has a differing inventive entity than the present application, and the same isolated nucleic acids are being claimed. Clarification is requested.

Claims 22, 23 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 49-55 of U.S. Patent No. 5,853,988. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are each drawn to methods of detecting mutants of a retinoblastoma nucleic acid through hybridization, and/ or sequencing. It is noted that the '988 patent has a differing inventive entity than the present application. Clarification is requested.

The examiner notes that Applicant wishes to hold these rejections in abeyance until allowability is noted, however, the examiner requests that the information regarding inventorship be provided in Applicant's response.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5,998,143 Lee et al. claims methods of detecting a mutant RB gene in a sample.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

The fax number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose telephone number is (703) 305-3524.

mkz
April 3, 2001

Mary K. Zeman
MARY K. ZEMAN
PATENT EXAMINER
AU 1631